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My comments are addressed to the RFI listed as:
http://www.gpo.gov/fdsys/pkg/FR-2011-10-11/pdf/2011-26088.pdf

Grand Challenges:

1. Rational basis for polypharmacy. HIV/AIDS needed a therapy based on simultaneous delivery of a cocktail of drugs, because of the virus' capacity for rapid evolution. Cancer presents the same problem. Successful treatments have evolved empirically using a cocktail of low specificity toxic drugs. The reductionist approach favored by molecular biologists, like myself, have focused on single, highly specific inhibitors, such as tyrosine kinase inhibitors. Efficacy is good but remission is almost universal. New developments in mammalian cell genetics, such as synthetic lethality, allows a rational approach to polypharmacy that will allow the use of a cocktail of drugs but each with high specificity.
2. Molecular signatures of disease. New developments, for example in using DNA sequencing to measure protein synthetic rates, allow the researcher to see even a 20% change in a protein marker in response to a disease, thus laying the foundation for protein based, molecular diagnosis of most if not all the major human diseases. Although this is especially needed for Alzheimer's disease, it can be of value across disease categories. Since NIH is structured to focus on diseases, such a pan-disease effort to develop molecular signatures may need a restructuring equivalent to that needed for the Human Genome Project.
3. DNA sequencing for PHENOTYPIC analysis. Much current focus is on the $1,000 genome. Our genome certainly contributes to our disease proclivities but our environment plays at least as significant a role. We need a greater emphasis on using new DNA sequencing capacity to detect pathogens in our body and to characterize our microbiome more extensively.

Research and development:

1. Align research investment more with medical need. Kidney disease and its treatment with dialysis, for example, is a major financial burden on our health care system. Funding for innovations that can replace our cumbersome and expensive dialysis systems is almost non-existent. Alzheimer's is a growing threat to our economy yet we invest more in HIV/AIDs than in Alzheimer's.
2. Support Research on Cost-reducing technologies. Current NIH funding supports improvements in the quality of health care. There is no funding category that supports technological advances that might make health care more accessible by reducing its cost. The private sector has little interest in such developments; for our continued economic viability as a nation, it is essential.
3. Reduce redundancies. A common criticism of NIH from outsiders is that many labs may be funded to do the same research. In times of austerity, reviewers should be alerted to the existence of other grants funding essentially the same work when setting funding priorities.

Lab to Market:

1. Modify NIH Funding Requests. Grant applications currently require the writer to define what diversity programs exist in their university. This has been a very successful strategy. If the NIH were to ask what the applying institution is doing to foster entrepreneurship, and how successful those steps have been, US universities would become hot-beds of entrepreneurship in a couple of years!
2. Support Academic Generalists. The current system favors specialization while innovations come from cross-disciplinary interactions. Academic institutions do not recruit generalists, those who are talented at assimilating vast amounts of information and seeing unexpected connections. They should.
3. University-associated incubators. Close association of budding entrepreneurs with the mother campus is of crucial importance in the first difficult year or two of company formation. Conversion of under-utilized university space to small incubator labs should be encouraged, for example, by removing legal and policy objections to commercial work on university campuses.

4. Small Business Grants. These are the life blood of lean start-ups. The money is so valuable that the government should resist pressures from the National Venture Association to use them as non-dilutive funding. If tensions exist between politicians who favor the creation of Mom-and-Pop retail stores in middle America and those who want to use such grants to stimulate innovation then a reconciliation effort should be mounted. These are the crown jewels of the NIH in our opinion.
5. Seed funding. Money for life science start-ups in notorious hard to find. One possibility is to allow research universities to apply for one-time loans with which to fund start-ups, with the idea that they should generate enough income from their investments that their program be self-sustaining.

Regulatory Barriers and Re-imbursement policies

1. Diagnostic devices. Modern treatment is moving rapidly towards companion diagnostics and, hopefully, molecular diagnoses of disease. Unfortunately venture funding for such areas is minimal, because of the poor return and the challenging regulatory environment for diagnostics. To improve the situation, the FDA should endorse the use in America of any diagnostic approved in Europe.
2. User driven innovation. The Defense department specifies the characteristics of a weapon it wants to be developed and may give a price it is willing to pay. The Government could revolutionize the industry if it would announce medical improvements it was seeking, acceptable side effect to benefit ratios and the price it would pay for a successful product or procedure.

Public-Private partnerships.

1. Science Hotels. The turmoil in the R&D divisions of major pharmaceutical firms is challenging them to seek inexpensive and effective alternatives. One possibility is to have satellites of companies locate next to major research universities in science hotels so that company and university scientists can work together to solve a major health problem. When the problem is solved the company would leave. Tax breaks might encourage companies to engage in such partnerships.
2. Regulatory Science Think-tanks. Objective, impartial entities are required to assess the value of regulatory processes and whether one regulation should be replaced by a more effective one. Creation of a National Regulatory Think-tank, independent of political or industry pressure, devoted to informed analysis of regulatory policy could be a national asset.

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